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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KAPUST, RACHEL B	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M. S.M.

Office Action Summary	Application No.	Applicant(s)	
	09/922,011	DAMBINOVA, SVETLANA A.	
	Examiner	Art Unit	
	Rachel B. Kapust	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *1-40 and 46-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,10*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group III, claims 41-45 in Paper No. 9 is acknowledged. Furthermore, Applicant's election of the NR2A NMDA receptor in the response dated September 22, 2003 is acknowledged. Claims 1-40 and 46-62 are withdrawn from consideration as being drawn to non-elected inventions. Claims 41-45 are under examination as they pertain to the elected species of NR2A NMDA receptor.

Specification

The use of the trademarks DNAZOL™, TWEEN-20™, and DELTAPAC™ have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claim 45 is objected to because of the following informalities: Claim 45 is drawn to a method wherein the level of NR2A NMDA receptor is measured from the amount of "autobody" against NR2A NMDA receptor. This appears to be a typographical error in that Applicant probably meant "autoantibody." Applicant refers to autoantibodies throughout the application, but Applicant never refers to autobodies. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 41-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for diagnosis of either a stroke or TIA, does not reasonably provide enablement for diagnosis of all central nervous system disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention; 2) state of the prior art; 3) relative skill of those in the art; 4) level of predictability in the art; 5) existence of working examples; 6) breadth of claims; 7) amount of direction or guidance by the inventor; and 8) quantity of experimentation needed to make and/or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Applicant teaches that NR2A NMDA receptor mRNA expression is associated with focal ischemia (p. 12), and levels of NR2A NMDA receptor are predictive of the occurrence of either stroke or TIA or risk of stroke (p. 13). However, Applicant has not provided examples of other central nervous system disorders with which NR2A NMDA receptor is known to be associated. The term "central nervous system disorder" encompasses a variety of disorders such as Parkinson's disease and Parkinsonian disorders, Huntington's disease, Alzheimer's disease, Amyotrophic Lateral Sclerosis, spinal ischemia, spinal cord injury and cancer-related brain/spinal cord injury, schizophrenia and other psychoses, depression, bipolar depression/disorder, cognitive function disorders, aggression, drug and alcohol abuse, obsessive compulsive behavior syndromes, seasonal mood disorder, borderline personality disorder, Cerebral palsy, multi-infarct dementia, Lewy body dementia, age related/geriatric dementia, spinal cord injury, brain injury, trauma related brain/spinal cord injury, anti-cancer treatment related brain/spinal cord tissue injury (radiation and cytostatics), infection and inflammation

related brain/spinal cord injury, environmental toxin related brain/spinal cord injury, multiple sclerosis, autism, attention deficit disorders, narcolepsy and sleep disorders. Many of theses disorders are still in their infancy of being understood. More importantly, it is not known whether NR2A NMDA receptor is associated with any of these disorders.

One of skill in the art would first need to determine whether or not NR2A NMDA receptor is associated with a disorder, and then one would be able to practice the method as taught by Applicant. Because of the lack of working examples, the breadth of the claims, and the lack of direction provided by the Applicants, it would require undue experimentation by one of skill in the art to practice the invention as claimed without further guidance from the instant specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 41-43 and 45 are rejected under 35 U.S.C. 102(b) as being unpatentable over Dambinova *et al.* (1997, *J. Higher Nervous Activity* 47(2): 151-156, submitted by Applicant in IDS dated February 26, 2002). Claims 41-43, and 45 are drawn to a method for diagnosing a central nervous system disorder by measuring the level of NR2A NMDA receptor and the level of one or more agonist or antagonist of the NR2A NMDA receptor. Dambinova *et al.* teach a direct method of detection of NR2A NMDA receptor by immunopurification (p. 152, column 2) and an indirect method of detection by detecting autoantibodies to NR2A NMDA receptor (p. 153, column 2) in stroke patients. Moreover, Dambinova *et al.* teach measuring glutamate and aspartate concentrations in stroke patients (p. 153, column 2). Therefore, Dambinova *et al.* anticipate claims 41-43 and 45.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dambinova *et al.* (1997), as discussed above, in view of Daggett *et al.* (U.S. Patents 6,316,611 and 5,849,895). Specifically, Dambinova *et al.* teach measuring the level of NR2A NMDA receptors in stroke patients by measuring the levels of autoantibodies to the receptors, an indirect method, and by measuring the amount of NR2A NMDA receptor directly by immunopurification, a direct method. However, Dambinova *et al.* do not teach a method of indirectly measuring the level of NR2A NMDA receptor in stroke patients by measuring the amount of NR2A NMDA receptor mRNA. In the 5,849,895 patent, Daggett *et al.* teach an indirect method of detection of NR2A NMDA receptor by detecting NR2A NMDA receptor mRNA (column 9, line 63 through column 10, line 12). Daggett *et al.* also teach an indirect method of RNA detection by identifying NR2A NMDA receptor cDNA (column 8, lines 26-39 in the 5,849,895 patent). It would have been obvious to a person of ordinary skill in the art to combine the methods as taught by Daggett *et al.* with the method as taught by Dambinova *et al.* One of ordinary skill in the art would have been motivated to do so because Dambinova *et al.* teach that detecting NR2A NMDA receptors are useful for diagnosing strokes, and the 5,849,895 and 6,316,611 patents teach alternative means of detecting NR2A NMDA receptors that one of ordinary skill in the art would have expected to be

equally useful. Therefore, the invention taken as a whole is *prima facie* obvious over the prior art.

Claims 41- 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dambinova *et al.* (1997, *J. Higher Nervous Activity*) in view of Lipton *et al.* (1997, *Proc. Natl. Acad. Sci. USA* 94: 5923-5928, submitted by Applicant in IDS dated February 26, 2002). As previously stated, Dambinova *et al.* teach both indirect and direct methods of measuring the level of NR2A NMDA receptor in stroke patients. Moreover, Dambinova *et al.* teach that measuring NR2A NMDA receptor levels is useful for diagnosing strokes. However, Dambinova *et al.* do not teach measuring homocysteine levels in stroke patients. Lipton *et al.* teach that there is an association between homocysteine and cerebrovascular disease and that it can directly cause neurotoxicity by activating NMDA receptors (p. 5923). Lipton *et al.* further teach that elevated levels of homocysteine in the blood are diagnostic of arteriosclerosis and stroke. Because each method is useful for the same purpose, it would be *prima facie* obvious to combine the two methods in order to form a combination that is to be used for the very same purpose. See *In re Kerkhoven* (205 USPQ 1069, CCPA 1980). One of ordinary skill in the art would have been motivated to combine the methods of Dambinova *et al.* and Lipton *et al.* because they are both useful for diagnosing strokes.

Conclusion

NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel B. Kapust whose telephone number is (703) 305-0634. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm. Please note for your records that as of approximately January 20, 2004, the examiner's new telephone number will be (571) 272-0886.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RBK
12/03